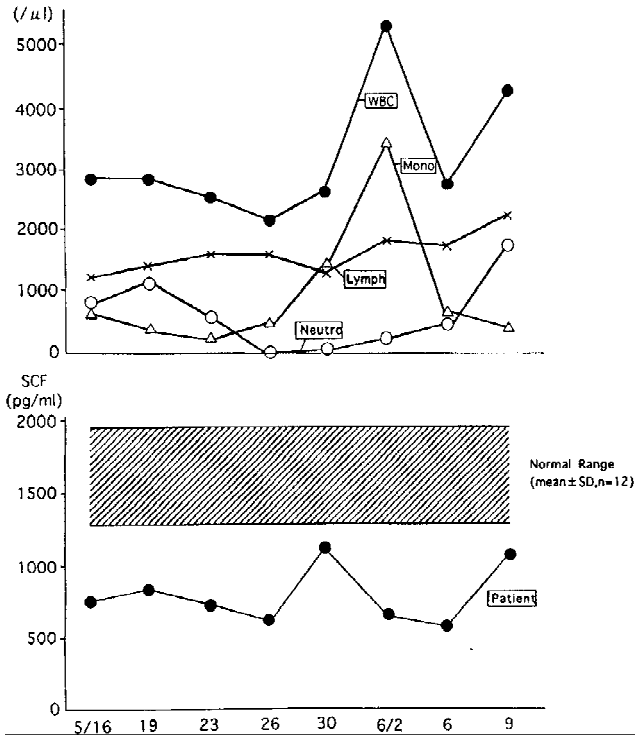

Fig. 1. Top: Fluctuations in hematological values. Bottom: Levels of plasma-soluble stem-cell factor (SCF). Mean value of duplicate determinations is shown.

uct in cyclic neutropenia, may more directly demonstrate the function of bone-marrow stromal cells in this disorder.

KENJI SHINOHARA
KOUICHI ARIYOSHI
KOUMEI TAKEDA
NAOKO KAMEDA
XU RUIRONG

Division of Hematology, Department of Medicine, Yamaguchi Prefecture Central Hospital, Hofu, Japan

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Erythropoietin Permits High-Dose Chemotherapy With Peripheral Blood Stem-Cell Transplant for a Jehovah's Witness

To the Editor: Due to their religious conviction prohibiting the receipt of blood products, Jehovah's Witnesses with leukemia and lymphoma preclude themselves from many of the more aggressive neoplastic treatments, such as high-dose chemotherapy. Although Jehovah's Witnesses safely undergo major operative procedures and standard-dose chemotherapy, there are very few reports of these individuals being offered more intensive marrow-ablative chemotherapy, even in potentially curative situations. One previous case describes the treatment of a Jehovah's Witness with high-dose cytarabine after a second relapse of his acute monocytic leukemia [1]. High-dose chemotherapy, even with bone-marrow or peripheral blood stem-cell support, places patients at risk for infections and bleeding complications directly related to treatment-induced profound and prolonged pancytopenia, typically requiring multiple blood and platelet transfusions. Jehovah's Witnesses are often denied these procedures because of the fear of unacceptable mortality rates. In those patients unwilling to accept blood transfusions, various supportive techniques, including the glycoprotein hormone erythropoietin, may safely allow more aggressive treatment options [2].

We treated a 30-year-old Jehovah's Witness with recurrent non-Hodgkin's lymphoma (NHL) with high-dose chemotherapy, followed by autologous peripheral stem-cell transplant. This patient was first diagnosed with intermediate grade, B-cell non-Hodgkin's lymphoma. He received three months of VACOP-B chemotherapy with doxorubicin, cyclophosphamide, prednisone, bleomycin, vincristine, and etoposide, followed by 4,050 rads of radiation therapy. Seven months later, this patient returned with a large renal mass. Salvage chemotherapy with four cycles of decadron, ifosphamide, cisplatin, and etoposide induced a second remission.

After much discussion of the possible risks, this patient decided to undergo high-dose chemotherapy with peripheral stem-cell support. Cells were harvested by apheresis, with 5 mcg/kg of G-CSF growth factor administered twice daily for mobilization. He was then admitted to the hospital where he underwent an intensive chemotherapy regimen consisting of 6 g/m^2 cyclophosphamide, 2,100 mg/m^2 etoposide, and 300 mg/m^2 carmustine (BCNU) over 5 days. This individual was reinfused with 7.28×10^8 mononuclear cells/kg, consisting of 10.5×10^6 CD34$^+$ cells/kg and 90×10^4 colony-forming units/kg. In an attempt to avoid profound anemia, he was given 10,000 units of erythropoietin every day with 325 mg of ferrous sulfate three times a day, beginning 2 weeks prior to his high-dose chemotherapy. To limit iatrogenic blood loss, tests were performed every other day, drawing only 1–2 ml into pediatric vials. To prevent bleeding during the period of thrombocytopenia he was given 2 g of aminoceaproic acid every 6 hr.

In this patient, erythropoietin priming stimulated red blood cell production within the first 2 weeks of administration, as evidenced by an increase in his hemoglobin from 8.8 g/dl to 11.7 g/dl. The patient's blood counts were monitored as an outpatient during the engraftment period, with the lowest hemoglobin value of 9.7 g/dl seen on day 13 following reinfusion. For our prior 8 patients undergoing this procedure without erythropoietin priming, the hemoglobin fell an average of 5.4 g/dl below baseline, as compared to his 2 g/dl decrease, with 6 of the prior patients requiring transfusions. The present patient's absolute neutrophil count (ANC) rose above 1,000 on day 8 after reinfusion while platelets reached 20,000 on day 9, and 50,000 on day 13. After 50 days, he was able to resume an exercise program with a hemoglobin level at 12.9 g/dl. The patient experienced no major complications during the transplant directly related to anemia or thrombocytopenia.

Erythropoietin has the potential to reduce or limit blood transfusions, following high-dose chemotherapy. If hemoglobin levels can be elevated before and during the 2-week engraftment period, unnecessary or undesired blood transfusions can be avoided. The ability to predict if and how rapidly a patient will experience accelerated erythrocyte production from erythropoietin, so that the minimum time course and optimal dosage can be

administered to reduce the drug's cost, remains to be determined. This case demonstrates that a short-term regimen of erythropoietin and iron supplementation may allow high-dose chemotherapy to be offered to those individuals unwilling to accept blood products.

Jason Todd Estrin
Department of Molecular Biology, Princeton University, Princeton, New Jersey

Patricia A. Ford
David H. Henry
Arthur P. Stradden
Bernard A. Mason
Oncology Hematology Associates, The Graduate Hospital, Medical School of the University of Pennsylvania, Philadelphia, Pennsylvania

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Chronic Lymphocytic Leukemia Supervening in Non-Hodgkin's Lymphoma (Diffuse, Mixed-Cell Type)

To the Editor: Several reports have documented patients exhibiting different histologic subtypes of non-Hodgkin's lymphoma (NHL) in multiple sites (discordant lymphoma), or in a single tumor mass (composite lymphoma) [1,2]. However, few authors have clarified whether such lymphomas presenting with divergent histologic subtypes arise from a original common clone or from distinct malignant clones [3]. Related phenomena have been observed in Richter's syndrome, in which large-cell lymphoma supervenes in patients with chronic lymphocytic leukemia (CLL). Several authors have reported on immunophenotypic and immunogenotypic analyses regarding the clonal relationship between CLL and large-cell lymphoma, and it is generally considered that two morphologically distinct neoplasms were evoluted from the same clone [4,5]. Our case of CLL arising in a patient with long-standing NHL (diffuse, mixed-cell type) showed the reverse pattern, in which the lowgrade component supervened in the course of high-grade lymphoma. We examined the clonal relationship of these two malignancies by a combination of immunophenotypic and immunogenotypic analysis.

In October 1988, a 62-year-old man had general lymphadenopathy. He had diffuse lymphadenopathy up to 2 cm in the cervical, axillary, and inguinal regions, but no hepatosplenomegaly. At that time, results of a blood workup were as follows: hemoglobin level, 14.7 g/dl; leukocyte count, 9,200/μl (neutrophils 62%, lymphocytes 27%); and platelet count, $21.9 \times 10^4/\mu l$. An abdominal computed tomographic scan and gallium scan revealed diffuse lymphadenopathy in the cervical, axillary, inguinal, and periaortic regions. Rt-cervical lymph node biopsy showed NHL (diffuse, mixed-cell type). Immunophenotypic analysis of lymph-node cell suspensions showed a preponderance of CD5(−), CD19(+), CD20(+), and surface Ig(−) cells. Bone-marrow aspiration was normal. He was admitted to hospital and treated with combined chemotherapy (vincristin, cyclophosphamide, prednisone, and doxorubicin), resulting in partial remission.

Although an abdominal computed tomographic scan after chemotherapy revealed residual lymphadenopathy in the periaortic regions, surface lymph

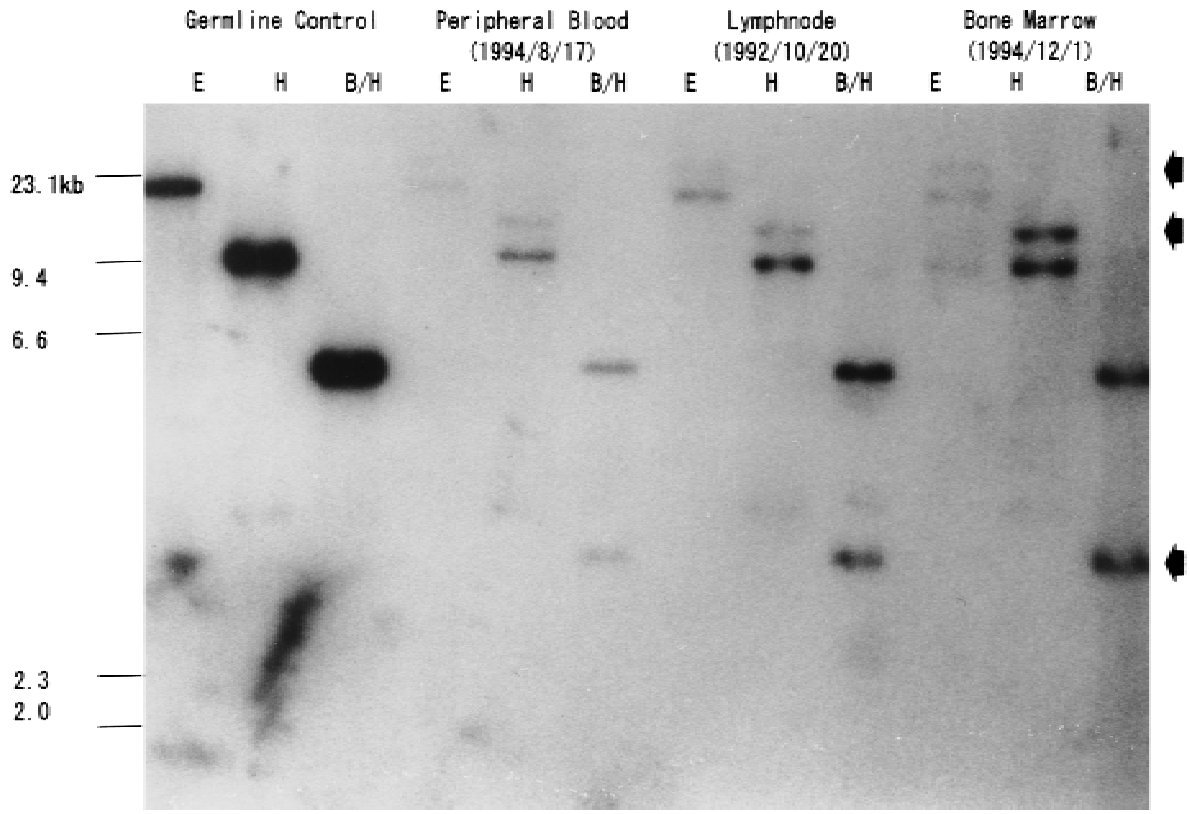

Fig. 1. Immunoglobulin (Ig) gene rearrangement analysis of DNA from lymph node (October 1992), peripheral blood cells (August 1994), and bone marrow (December 1994), using a probe to the joining region of the Ig heavy-chain gene (J_H). DNAs were digested with *Eco*RI (E), *Hind*III (H), and *Bam*HI/*Hind*III (B/H) restriction enzymes. Arrows indicate rearranged bands.